Energy Metabolism of Dopaminergic Neurons in Microfluidic Cell Culture

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Principal Investigators

Edinson Lucumi-Moreno

Institution

Université du Luxembourg

Contact information of lead PI
Country

Luxembourg

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Energy Metabolism of Dopaminergic Neurons in Microfluidic Cell Culture

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Research Abstract

Dopaminergic neurons (DA) play a central role in brain function. The loss of DA neurons from the substantia nigra pars compacta (SNc) is responsible for the pathophysiology of Parkinson?s disease (PD). It is estimated that the number of DA neurons in human SNc is in the realm of 382,000 and each DA neuron can give rise to 1 to 2.4 million synapses at the level of the striatum with total axon length of up to 4.5 meters. These morphological characteristics make DA neurons uniquely vulnerable in neurodegenerative diseases. The high energy demand of SNc DA neurons, due to their morphological and functional characteristics, is considered to be an important factor in the susceptibility of DA neurons in PD. Cellular models of PD are limited

by the access to in vitro culture of affected human DA neurons. Stable cell lines of Neuroepithelial stem cells (NESC) originated from patients, offer a unique opportunity to obtain DA neurons (10% to 70% efficiency) using small molecules. DA neurons with LRRK2 mutation resemble the familial form of PD. Microfluidic cell culture and calcium imaging offers an unique approach to study cellular differentiation and energy metabolism in DA neurons. In this project, we aim to implement a microfluidic cell culture platform at LCSB to culture DA neurons and by using calcium imaging, quantify the degree of differentiation and electrophysiological demand on energy metabolism. The acquired data will be used as a constraint on energy metabolism in computational model of a dopaminergic neuron. We shall apply control theory and experimental automation to optimize the existing protocol for the differentiation of neuroepithelial stem cells into dopaminergic neurons using small molecules. We shall compare the electrophysiological and morphological phenotyping of NESC stable cell lines derived dopaminergic neurons from healthy individuals and patients with sporadic and familial PD.

Further information available at:

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